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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,962	09/08/2003	Mendy S. Maccabee	49321-102	3139
22504	7590	10/28/2008		
DAVIS WRIGHT TREMAINE, LLP/Seattle			EXAMINER	
1201 Third Avenue, Suite 2200			KIM, JENNIFER M	
SEATTLE, WA 98101-3045			ART UNIT	PAPER NUMBER
			1617	
			MAIL DATE	DELIVERY MODE
			10/28/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/658,962	MACCABEE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	JENNIFER M. KIM	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 27 August 2008.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-8, 11, 12 and 21 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-8, 11, 12 and 21 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____ .	6) <input type="checkbox"/> Other: _____ .

## **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 27, 2008 has been entered.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 7 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board

of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 11 recites the broad recitation "**vitamin A**", and the claim also recites "**retinoic acid**" which is the narrower statement of the range/limitation; Claim 2 recites the broad recitation "ciliated epithelial structure", and the claim also recites "**including** respiratory epithelium" which is the narrower statement of the range/limitation; and claim 7 recites the broad recitation "an indicator", and the claim also recites "**including** of the lamina propria... **including** causing a greater density.... **including** sinus bone morphometry" which is the narrower statement of the range/limitation.

#### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8, 11, 12 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biesalski (U.S. Patent No. 5,556,611) of record in view of Belloni (U.S. Patent No. 6,339,107 B1) of record.

Biesalski teaches a pharmaceutical preparation consisting of **retinoic acid** as an active substance suitable for a topical treatment of mucosal disease in man and animal. (abstract). Biesalski teaches the preparation can be formulated in an aerosol formulation. (abstract). Biesalski teaches the effective amount of the active substance is from 0.01-50% by weight. (column 6, line 44). This range encompasses and touches Applicants' amounts set forth in claim 8. Biesalski teaches that the preparation is effective for treating functional impairments in the mucous membranes of humans and animals, in particular in the respiratory epithelium and the epithelia of the nose-throat cavity. Biesalski teaches that the treatment is also useful in reduced activity of the ciliated epithelium and disturbances of the mucous membranes of the respiratory tract. (column 10, lines 24-45). Biesalski teaches the preparation is effective for treating acute and chronic bronchitis, acute and chronic functional disturbances due to impairment of tracheobronchial epithelium and bronchopulmonary dysplasia.

Biesalski do not expressly teach the non-aerosol, depot formulation of retinoic acid, and the cause of the ciliated epithelial structure damage due to the surgical intervention.

Belloni teaches a composition comprising retinoic acid for the treatment of emphysema including the airspaces distal to the terminal bronchioles and destruction of their walls. (abstract, column 4, lines 50-60). Belloni teaches that topical administration

of retinoic acid can be formulated as solutions, gels, ointments, creams, suspension, etc. as are well-known in the art. (column 8, lines 14-17). Belloni teaches that retinoic acid can be formulated for oral liquid preparations such as suspensions, elixirs and solutions, as well as transmucosal and buccal administration. (column 8, lines 35-40, line 40-65, column 9, lines 1-6). Belloni teaches that retinoic acid can be formulated as a **depot preparation**. (column 10, lines 35-45).

It would have been obvious to one of ordinary skill in the art to modify the aerosol formulation of retinoic acid taught by Biesalski to topical non-aerosol, depot formulations such as solution, ointments and transdermal as taught by Belloni for the treatment of damaged ciliated epithelial structure. One would have been motivated to make such a modification because Belloni teaches that retinoic acid can be formulated for the treatment of damaged respiratory walls and because such damaged respiratory walls are routinely treated with depot preparations and various topical formulations comprising retinoic acid as taught by Belloni et al. There is a reasonable expectation of success in treating a damaged ciliated epithelial structure comprising topical administration of non-aerosol such as ointment comprising retinoic acid because such formulation and the method of treating damaged or destruction of respiratory walls are well known in view of Belloni.

It would have been obvious to one of ordinary skill in the art to employ retinoic acid preparation taught by Biesalski as modified by Belloni for the treatment of damaged ciliated epithelial structure regardless of cause because both Biesalski et al. and Belloni teach that the retinoic acid preparation is effective for the treatment of impaired ciliated

epithelium and damaged respiratory walls. One would have been motivated to employ the retinoic acid preparation taught by Biesalski as modified by Belloni for a condition of damaged ciliated epithelium or damaged respiratory at any cause including the surgical intervention in order to treat the condition or the symptoms of damaged ciliated epithelium at any cause including the damage from the surgical intervention. There is a reasonable expectation of successfully treating damaged ciliated epithelium because both Biesalski and Belloni teach the effectiveness of the preparation in repairing and treating damaged ciliated epithelium or damaged respiratory walls in man or animal with retinoic acid.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

### **Response to Arguments**

Applicants' arguments filed August 27, 2008 have been fully considered but they are not persuasive. Applicants argue that Belloni teaches away from using retinoic acid also known as all-trans-retinoic acid (ATRA) in its formulations because Belloni teaches that the use of ATRA in treating emphysema is undesirable because the compound

presents several toxicity concerns. Applicants further argues that Belloni provides data in Table 6 (top of column 15) that demonstrates the higher therapeutic index of 13-cis-retinoic acid as compared to ATRA that ATRA is substantially less effective than 13-cis-retinoic acid in repairing alveoli at low dosages. This is not found to be persuasive because Biesalski teaches that a pharmaceutical preparation consisting of **retinoic acid** as an active substance suitable for a topical treatment of mucosal disease in man and animal; and the treatment is useful in reduced activity of the ciliated epithelium and disturbances of the mucous membranes of the respiratory tract and also useful in chronic functional disturbances due to impairment of tracheobronchial epithelium and bronchopulmonary dysplasia. Therefore, Biesalski teaches that retinoic acid in general is useful for such treatment does not limit retinoic acid to only all-trans-retinoic acid (ATRA). One of ordinary skill in the art would immediately envision that retinoic acid taught by Biesalski is known to exist in different geometric isomeric form particularly two retinoids such as tretinoin (all-trans retinoic acids) and isotretinoin (13-cis retinoic acid) for a certain topical treatment. Although Belloni may teach that 13-cis-retinoic acid compared to retinoic acid in its formulation does not change the relevant teaching from Biesalski that retinoic acid inclusive of various isomeric forms effective in treatment of condition associated with ciliated epithelium. In response to applicant's argument of Belloni's 13-cis-retinoic acid providing better result compared to all-trans retinoic acid, it does not change that both compounds 13-cis-retinoic acid and all-trans retinoic acid are known in the art as a retinoic acid. Applicants argue that Biesalski describes aerosol formulations containing ATRA (retinoic acid) for treating disorders of mucous

membranes. This is not found to be persuasive because Biesalski does not limit his vitamin A compound to "ATRA" or only to "all-trans-retinoic acid". Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

### **Communication**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Jennifer Kim/  
Primary Examiner, Art Unit 1617

October 18, 2008